REMARKS

Claims 1-7 are pending in this application. Claims 2-7 have been withdrawn from consideration. Claim 1 has been rejected. Claims 1-7 have been canceled. Claim 8 has been added. No new matter has been added. Applicants are respectfully requesting reconsideration in view of the following remarks.

I. Election/Restrictions

The Restriction Requirement mailed August 6, 2009 has been deemed proper and made final. Claims 2-7 have been withdrawn from further consideration. Accordingly, Applicants have canceled claims 2-7 without prejudice reserving the right to file continuing applications for the canceled subject matter.

II. Rejection of the Claims Under §112

Claim 1 has been rejected under 35 U.S.C. 112, first paragraph. The Examiner suggests that while the specification enables a method for identifying an agent which destabilizes lysosomes, the specification does not reasonably enable a method for identify an agent that destabilizes lysosomes and increases any oncogenic or aberrant protein degradation. It is suggested that the disclosure provides teachings directed to the exposure of cell lysates or isolated lysosomes being contacted with arsenic and observation of degradation of (oncogenic) PML/RARa or (aberrant) CFTR proteins in the reaction mixtures, but does not teach examples of any other agents having this property. It is suggested that the disclosure does not indicate a concomitant increase in protein degradation of either oncogenic or aberrant

proteins in response to chloroquine, nor if chloroquine actually destabilizes lysosomes at all. The Examiner concludes that one of ordinary skill in the art would have to test innumerable compounds both for lysosomal destabilizing properties as well as protein degradation as not all destabilizing agents increase protein degradation of aberrant or oncogenic proteins.

Applicants respectfully disagree with this rejection. Applicants have demonstrated that destabilization of lysosomes results in an increase in the degradation of PML/RARα protein. See the passage spanning page 4 (line 22) and page 5 (line 14). Applicants appreciated that these findings serve as a basis for a screening assay to identify other agents that destabilize lysosomes and degrade oncogenic proteins such as PML/RARα. In this respect, the passage spanning page 8 (line 21) and page 12 (line 30) describes assays, reagents, and sources of candidate agents that can be screened using the method of this invention. Moreover, the passage spanning page 4 (line 22) and page 5 (line 14) describe methods for determining the degradative state of PML/RARα.

Accordingly, in an earnest effort to highlight the use of destabilized lysosomes and PML/RARα in screening assays, Applicants have canceled claim 1 and added new claim 8, which requires contacting a cell that expresses PML/RARα with an agent and detecting whether said agent destabilizes the lysosome and increases PML/RARα protein degradation. Support for new claim 8 is found in the passage spanning page 4 (line 22) and page 5 (line 14), and the passage spanning page 8 (line 21) and page 12 (line 30).

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). "That *some* experimentation may be required is not fatal; the issue is whether the amount of experimentation required is 'undue.'" *In re Vaeck*, 947 F.2d 488, 495 (Fed. Cir. 1991) (emphasis in original). Some experimentation, even a considerable amount, is not "undue" if, for example, the specification provides a reasonable amount of guidance as to the direction in which the experimentation should proceed. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

In so far as the Specification describes assays and reagents of use in the instant method, as well as candidate compounds that can be screened, undue experimentation would not be required to make and use the method as currently presented. Accordingly, the enablement requirement has been met for the screening method presented in claim 8. It is therefore respectfully requested that this rejection be reconsidered and withdrawn.

Claim 1 has also been rejected under 35 U.S.C. 112, second paragraph. It is suggested that claim 1 refers to the "destabilization" of lysosomes, however, it is unclear whether "destabilization" refers to physical disruption of the lysosomal membrane or any disruption of the lysosome. The Examiner has interpreted "destabilization" as any disruption of the lysosome activity or physical state.

In an earnest effort to clarify what is meant by the destabilization of a lysosome, new claim 8 specifies that lysosome destabilization is detected by vital staining of lysosomes or release of lysosomal proteins into the cytosol as supported by the disclosure spanning page 8 (line 21) and page 9 (line 2) of the Specification. In light of this clarification, it is respectfully requested that this rejection under 35 U.S.C. 112, second paragraph, be reconsidered and withdrawn.

III. Rejection of the Claims Under §102

Claim 1 has been rejected under 35 U.S.C. § 102(b) as being anticipated by Schütt et al. (2002). It is suggested that Schütt et al. teach that isolated, intact lysosomes can be destabilized (lysosomal membranes disrupted) by exposure to the lipofuscin retinoid component A2-E (N-retinylidene-N-retinylethanolamine) at concentrations above 2 µM.

Claim 1 has been rejected under 35 U.S.C. 102(b) as being anticipated by Öllinger et al. (1995). Öllinger et al. is suggested to teach a method wherein cultured, rat hepatocytes containing lysosomes are contacted with napthazarin (5,8-dihydroxy-1,4-napthoquinone) and detecting whether the napthazarin destabilizes the lysosomes by monitoring acridine orange fluorescence.

Claim 1 has been rejected under 35 U.S.C. 102(b) as being anticipated by Weeks et al. (1996). It is suggested that Weeks et al. teach a method wherein test earthworms are exposed to copper containing soil and coelomocytes containing lysosomes are extracted and detection of whether the copper destabilizes the

lysosomes is performed by monitoring neutral red uptake and loss by lysosomes.

The Examiner concludes that the A2-E compound of Schütt et al., the napthazarin compound of Öllinger et al., and the copper compound of Weeks et al. meet the limitations of the claimed invention, that is, an agent being able to destabilize the lysosome, wherein the limitation of increasing oncogenic or aberrant protein degradation is an inherent feature of these compounds as the claim only requires contacting a lysosome with an agent and detecting whether said agent destabilizes the lysosome.

MPEP 2131 instructs:

> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The method of the invention, as currently presented in new claim 8, requires detecting lysosome destabilization and increases in PML/RARα degradation. Neither Schütt et al., Öllinger et al., nor Weeks et al. teach or suggest all the elements of claim 8 as currently presented. These references therefore cannot be held to anticipate the present invention. It is therefore respectfully requested that these rejections under 35 U.S.C. 102(b) be reconsidered and withdrawn.

IV. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. According, favorable reconsideration and subsequence allowance of the pending claims is earnestly solicited.

Respectfully submitted,

Jane Massey Licata
Registration No. 32,257

Date: **February 23, 2010**

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, New Jersey 08053
(856) 810-1515
Email: jmlicata@licataandtyrrell.com